



PHYSICIANS' BULLETIN

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"Focusing on Families as Our Customers"

No. 451

Influenza Immunization Recommendations for 2004-2005

Note: Medicare B reimburses for influenza vaccines.

Influenza is a viral respiratory illness which is mainly spread through sneezing and coughing. Each year in the United States about 36,000 people die due to influenza and its complications. Administration of influenza vaccine is the primary method for preventing flu and its severe complications. Both the inactivated influenza vaccine and live, attenuated influenza vaccine (LAIV) can be used to reduce the risk of influenza. The 2004-05 trivalent vaccine contains A/Fujian/411/2002 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Shanghai/361/2002-like antigens (see #4 below). Significant updates are summarized here:

1. The American Academy of Family Physicians (AAFP), American Academy of Pediatrics (AAP) and the Advisory Committee on Immunization Practices (ACIP) recommend that **all children aged 6-23 months, and close contacts of children aged 0-23 months, be vaccinated against influenza.** These children have one of the highest rates of hospitalization due to influenza. (See **Influenza and Immunization Resources** later in this Bulletin for recommendations and strategies).
2. Inactivated vaccine is preferred over live, attenuated influenza vaccine (LAIV) for vaccinating household members, health care workers (HCWs), and others who have close contact with severely immunosuppressed persons during periods when such persons require care in a protected environment. If an HCW receives LAIV, the HCW should refrain from contact with severely immunosuppressed patients for 7 days after vaccine receipt. No preference exists for inactivated vaccine use by

HCWs or other persons who have close contact with persons with lesser degrees of immunosuppression (see **Live Attenuated Influenza Vaccine Recommendations**).

3. Severely immunosuppressed persons should not administer LAIV. However, other persons at high risk for influenza complications may administer LAIV (see **Personnel Who May Administer LAIV**).
4. Both LAIV and inactivated influenza vaccine contain the 3 strains of influenza viruses that are antigenically equivalent to the annually recommended strains. See the Table below for dosages and antigenically equivalent viruses. Influenza illness from the A/Fujian strain was predominant in the 2003-2004 season.

Target Groups for Vaccination 2004-2005

Both the inactivated influenza vaccine and LAIV can be used to reduce the risk of influenza. LAIV is only approved for use among healthy persons aged 5-49 years. Inactivated influenza vaccine is approved for persons aged ≥6 months, including those with high-risk conditions.

Persons at Increased Risk for Complications

Vaccination with inactivated influenza vaccine is recommended for the following persons who are at increased risk for complications from influenza:

1. children aged 6-23 months;

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Table 1: Inactivated Influenza Vaccine* Dose By Age Group, 2004-2005

Age group	Dose	Number of doses	Route§
6-35 mos.	0.25 mL	1 or 2¶	Intramuscular
3-8 yrs.	0.50 mL	1 or 2¶	Intramuscular
≥9 yrs.	0.50 mL	1	Intramuscular

* A 0.5-mL dose contains 15 µg each of A/Fujian/411/2002 (H3N2)-like, A/New Caledonia/20/99 (H1N1)-like, and B/Shanghai/361/2002-like antigens. For the A/Fujian/411/2002 (H3N2)-like antigen, manufacturers may use the antigenically equivalent A/Wyoming/3/2003 (H3N2) virus, and for the B/Shanghai/361/2002-like antigen, manufacturers may use the antigenically equivalent B/Jilin/20/2003 virus or B/Jiangsu/10/2003 virus. Manufacturers include Aventis Pasteur, Inc. (Fluzone® split virus); and Chiron (Fluvirin® purified surface antigen vaccine). Fluzone is approved by the Food and Drug Administration for use among persons aged ≥6 months. Fluvirin is approved for use only among persons aged ≥4 years. For further product information, call Aventis Pasteur at 800-822-2463 or Chiron at 800-200-4278.

§ For adults and older children, the recommended site of vaccination is the deltoid muscle. The preferred site for infants and young children is the anterolateral aspect of the thigh.

¶ Two doses administered at least 1 month apart are recommended for children aged <9 years who are receiving influenza vaccine for the first time.

Persons at Increased Risk for Complications (cont.)

2. persons aged ≥ 50 years;
3. residents of nursing homes and other chronic-care facilities that house persons of any age who have chronic medical conditions;
4. adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including asthma;
5. adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic diseases (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus [HIV]);
6. children and adolescents (aged 6 months–18 years) who are receiving long-term aspirin therapy and, therefore, might be at risk for experiencing Reye syndrome after influenza infection;
7. women who will be pregnant during the influenza season.

Because of the increased risk for influenza-related complications, women who will be pregnant during the influenza season should be vaccinated. Vaccination can occur in any trimester. One study of influenza vaccination of $>2,000$ pregnant women demonstrated no adverse fetal effects associated with influenza vaccine.

Children Aged 6 through 23 Months

Because children aged 6-23 months are at substantially increased risk for influenza-related hospitalizations, AAFP, AAP and ACIP recommend vaccination of all children in this age group. All continue to recommend influenza vaccination of persons aged ≥ 6 months who have high-risk medical conditions. The current inactivated influenza vaccine is not approved by FDA for use among children aged <6 months, which is the pediatric group at greatest risk for influenza-related complications. Vaccinating their household contacts and out-of-home caregivers might decrease the probability of influenza infection among these children.

The Vaccines For Children (VFC) program was expanded to include all VFC-eligible children aged 6-23 months and VFC-eligible children aged 2-18 years who are household contacts of children aged 0-23 months.

Persons Aged 50–64 Years

Influenza vaccine has been recommended for this entire age group to increase the low vaccination rates among persons in this age group with high-risk conditions. Age-based strategies are more successful in increasing vaccine coverage than patient-selection strategies based on medical conditions. Further, 50 years is an age when other preventive services begin and when routine assessment of vaccination and other preventive services has been recommended.

Persons Who Can Transmit Influenza to Those at High Risk

HCWs and close contacts should be vaccinated against influenza annually. Persons who are clinically or subclinically infected with influenza disease can transmit influenza virus to persons at high risk for complications from influenza. Decreasing transmission of influenza from caregivers and household contacts to persons at high risk might reduce influenza-related deaths among

persons at high risk. Evidence from two studies indicates that vaccination of healthcare personnel is associated with decreased deaths among nursing home patients. (See **Influenza and Immunization Resources** for links to web sites with guidelines.)

The following groups should be vaccinated:

1. physicians, nurses, and other personnel in both hospital and outpatient-care settings, including medical emergency response workers (e.g., paramedics and emergency medical technicians);
2. employees of nursing homes and chronic-care facilities who have contact with patients or residents;
3. employees of assisted living and other residences for persons in groups at high risk;
4. persons who provide home care to persons in groups at high risk;
5. household contacts (including children) of persons in groups at high risk.

In addition, because children aged 0–23 months are at increased risk for influenza-related hospitalization, vaccination is recommended for their household contacts and out-of-home caregivers, particularly for contacts of children aged 0–5 months, because influenza vaccines have not been approved by FDA for use among children aged <6 months. Healthy persons aged 5–49 years in these groups who are not contacts of severely immunosuppressed persons can receive either LAIV or inactivated influenza vaccine. All other persons in these groups should receive inactivated influenza vaccine. Use of LAIV or inactivated vaccine is further discussed in **Influenza Vaccine for Close Contacts of Persons at High Risk for Complications from Influenza**.

Importance of Vaccinating Health Care Workers

Influenza immunization rates among HCWs must be increased.

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The Centers for Disease Control and Prevention (CDC) as well as other infection control and major medical and nursing groups have long recommended yearly influenza vaccination for all HCWs, yet <40% are actually immunized each year. A comprehensive, concerted effort by health care institutions, employers, insurers and allied professional organizations is essential to improve HCW influenza vaccination rates. Beginning in October each year, health care facilities should provide influenza vaccine to all personnel, including night and weekend staff. Those employees should have convenient access to the vaccine at the work site, free of charge, as part of employee health programs. This will protect HCWs, their patients, and communities, and will improve prevention, patient safety, and reduce disease burden. Measuring and reporting HCWs' immunization rates is important. Although rates of HCW vaccination are typically <40%, with moderate effort, organized campaigns can attain higher rates of vaccination among this population.

Top management/administration need to become strong advocates to ensure HCWs become vaccinated in order to accomplish better infection control, cost savings, and reduced absenteeism. In this 2004–2005 season, many resources are available. (See the **Influenza and Immunization Resources**).

Strategies for Implementing Vaccination Recommendations in Health Care Settings

Successful vaccination programs combine publicity and education for HCWs and other potential vaccine recipients, a plan for identifying persons at high risk, use of reminder/recall systems, and efforts to remove administrative and financial barriers that prevent persons from receiving the vaccine. Suggestions for implementation in a variety of settings are detailed in the CDC's *Morbidity and Mortality Weekly Report* on influenza (MMWR 2004;Vol. 53:RR-6).

Additional Information Regarding Vaccination of Specific Populations

Breastfeeding Mothers

Influenza vaccine does not affect the safety of mothers who are breastfeeding or their infants. Breastfeeding does not adversely affect the immune response and is not a contraindication for vaccination.

Travelers

Persons at high risk for complications of influenza who were not vaccinated with influenza vaccine during the preceding fall or winter should consider receiving influenza vaccine before travel if they plan to travel to the tropics, travel with organized tourist groups at any time of year, or travel to the Southern Hemisphere during April–September. Persons aged ≥ 50 years and others at high risk should consult with their physicians before embarking on travel during the summer to discuss the symptoms and risks for influenza and the advisability of carrying antiviral medications for either prophylaxis or treatment of influenza.

General Population

In addition to the groups for which annual influenza vaccination is recommended, physicians can administer influenza vaccine to any person who wishes to reduce the likelihood of becoming ill

with influenza, depending on vaccine availability (see **Optimal Timing of Influenza Vaccine Activities**). Persons who provide essential community services should be considered for vaccination to minimize disruption of essential activities during influenza outbreaks. Students or other persons in institutional settings (e.g., those who reside in dormitories) should be encouraged to receive vaccine to minimize the disruption of routine activities during epidemics.

Persons listed in the paragraph above do not usually qualify for receipt of the California State-purchased influenza vaccine which is used for those at serious risk and their contacts. That vaccine is given in the County of San Diego Public Health Centers and in some other agencies.

Thimerosal and Influenza Vaccine

Thimerosal, a mercury-containing compound, has been used as a preservative in vaccines since the 1930s and is used in multidose vials of inactivated influenza vaccine to reduce the likelihood of bacterial contamination. Although no scientific evidence indicates that thimerosal in vaccines leads to serious adverse events in vaccine recipients, in 1999, the U.S. Public Health Service and other organizations recommended that efforts be made to eliminate or reduce the thimerosal content in vaccines to decrease total mercury exposure, chiefly among infants. Live, attenuated influenza vaccine does not contain thimerosal.

Thimerosal preservative-containing inactivated influenza vaccines, distributed in multidose containers in the United States, contain 25 mcg of mercury/0.5-mL dose. Inactivated influenza virus vaccines distributed in the United States as preservative-free vaccines in single-dose syringes contain only trace amounts of thimerosal (<1 mcg per 0.5 mL) as a residual from early manufacturing steps.

Beginning in 2004, influenza vaccine is part of the routine childhood immunization schedule. For the 2004–05 influenza season, 6–8 million single-dose syringes of inactivated influenza virus vaccine without thimerosal as a preservative will be available. This represents a substantial increase in the available amount of preservative-free inactivated influenza vaccine that was available in the 2003–04 influenza season. Inactivated influenza vaccine without thimerosal as a preservative is available from two manufacturers. Chiron produces Fluvirin®, which is approved by the Food and Drug Administration (FDA) for persons aged ≥ 4 years. Fluvirin is marketed as a formulation with thimerosal as a preservative in multidose vials and as a formulation without thimerosal as a preservative in 0.5-mL unit dose syringes. Aventis Pasteur produces Fluzone®, which is FDA-approved for persons aged ≥ 6 months. Fluzone containing thimerosal as a preservative is available in multidose vials. Preservative-free Fluzone packaged as 0.25-mL unit dose syringes is available for use among persons aged 6–35 months.

The risks of severe illness from influenza infection are elevated among both young children and pregnant women, and both groups benefit from vaccination by preventing illness and death from influenza. In contrast, no scientifically conclusive evidence exists of harm from exposure to thimerosal preservative-containing vaccine, whereas evidence is accumulating of lack of any

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harm resulting from exposure to such vaccines. **Therefore, the benefits of influenza vaccination outweigh the theoretical risk, if any, for thimerosal exposure through vaccination.**

Nonetheless, certain persons remain concerned regarding exposure to thimerosal. The U.S. vaccine supply for infants and pregnant women is in a period of transition during which thimerosal in vaccines intended for these groups is being reduced by manufacturers as a feasible means of reducing an infant's total exposure to mercury because other environmental sources of exposure are more difficult or impossible to eliminate. Reductions in thimerosal in other vaccines have been achieved already and have resulted in substantially lowered cumulative exposure to thimerosal from vaccination among infants and children. For all of these reasons, persons recommended to receive inactivated influenza vaccine may receive either vaccine preparation, depending on availability. Supplies of inactivated influenza vaccines without thimerosal as a preservative will be increased for the 2004–05 influenza season compared with the 2003–04 season.

Side Effects and Adverse Reactions of Inactivated Vaccine

When educating patients regarding potential side effects, clinicians should emphasize that 1) inactivated influenza vaccine contains noninfectious killed viruses and cannot cause influenza; and 2) coincidental respiratory disease unrelated to influenza vaccination can occur after vaccination. The Vaccine Information Statement (VIS), *Inactivated Influenza Vaccine, What You Need to Know, 2004-2005* (see **Influenza and Immunization Resources**) can be an effective tool to educate about side effects, risks and benefits.

Local Reactions with Inactivated Vaccine

In placebo-controlled studies among adults, the most frequent side effect of vaccination is soreness at the vaccination site (affecting 10%–64% of patients) that lasts <2 days. These local reactions typically are mild and rarely interfere with the person's ability to conduct usual daily activities. One blinded, randomized, cross-over study among 1,952 adults and children with asthma, demonstrated that only body aches were reported more frequently after inactivated influenza vaccine (25.1%) than placebo-injection (20.8%).

Systemic Reactions with Inactivated Vaccine

Fever, malaise, myalgia, and other systemic symptoms can occur after vaccination with inactivated vaccine and most often affect persons who have had no prior exposure to the influenza virus antigens in the vaccine (e.g., young children). These reactions begin 6–12 hours after vaccination and can persist for 1–2 days. Recent placebo-controlled trials demonstrate that among older persons and healthy young adults, administration of split-virus influenza vaccine is not associated with higher rates of systemic symptoms (e.g., fever, malaise, myalgia, and headache) when compared with placebo injections. Less information from published studies is available for children, compared with adults. However, in a randomized crossover study among both children and adults with asthma, no increase in asthma exacerbations was reported for either age group.

Health care professionals should promptly report all clinically

significant adverse events after influenza vaccination to VAERS (see **Influenza and Immunization Resources**), even if the health-care professional is not certain that the vaccine caused the event. Immediate, presumably allergic, reactions (such as hives, angioedema, allergic asthma, and systemic anaphylaxis) rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to certain vaccine components; the majority of reactions probably are caused by residual egg protein. Although current influenza vaccines, the LAIV as well as the inactivated, contain only a limited quantity of egg protein, this protein can induce immediate hypersensitivity reactions among persons who have severe egg allergy. Persons who have had hives or swelling of the lips or tongue, or who have experienced acute respiratory distress or collapse after eating eggs should consult a physician for appropriate evaluation to help determine if vaccine should be administered. Persons who have documented immunoglobulin E (IgE)-mediated hypersensitivity to eggs, including those who have had occupational asthma or other allergic responses to egg protein, might also be at increased risk for allergic reactions to influenza vaccine, and consultation with a physician should be considered. Protocols have been published for safely administering influenza vaccine to persons with egg allergies (see *Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices. MMWR 2004; Vol. 53:RR-6, p.14*)

Live, Attenuated Influenza Vaccine Recommendations

LAIVs have been in development since the 1960s in the United States. The LAIV licensed for use in the United States beginning in 2003 is produced by MedImmune, Inc. (Gaithersburg, Maryland; <http://www.medimmune.com>) and marketed under the name FluMist™. It is a live, trivalent, intranasally administered vaccine that is attenuated, producing mild or no signs or symptoms related to influenza virus infection. LAIV is approved for healthy persons age 5 years through 49 years. The vaccine is supplied in individual sprayers for nasal administration, and must be stored at –15°C or colder preferably in a manual-defrost freezer. LAIV virus strains replicate primarily in nasopharyngeal epithelial cells. The protective mechanisms induced by vaccination with LAIV are not completely understood but appear to involve both serum and nasal secretory antibodies. Possible advantages of LAIV include its potential to induce a broad mucosal and systemic immune response, its ease of administration, and the acceptability of an intranasal rather than intramuscular route of administration.

Shedding and Transmission of Vaccine Viruses.

Available data indicate that both children and adults vaccinated with LAIV can shed vaccine viruses for ≥2 days after vaccination, although in lower titers than typically occur with shedding of wild-type influenza viruses. Shedding should not be equated with person-to-person transmission of vaccine viruses, although, in rare instances, shed vaccine viruses can be transmitted from vaccinees to nonvaccinated persons.

Personnel Who May Administer LAIV

Low-level introduction of vaccine viruses into the environment is likely unavoidable when administering LAIV. The risk of acquiring vaccine viruses from the environment is unknown but likely

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to be limited. Severely immunosuppressed persons should not administer LAIV. However, other persons at high risk for influenza complications may administer LAIV.

LAIV Dosage and Administration

Details on storage, dosage, administration, side effects of LAIV are detailed at www.flumist.com, in the *MMWR Volume 53, RR-6*, as well as in the package insert. LAIV is intended for intranasal administration only and should not be administered by the intramuscular, intradermal, or intravenous route. LAIV must be stored at -15°C or colder, preferably in a manual-defrost freezer. Side effects can include runny nose and headache.

Persons Who Should Not Be Vaccinated with LAIV

LAIV is **contraindicated** for persons aged <5 years or those aged ≥ 50 years, persons with asthma, reactive airways disease or other chronic disorders of the pulmonary or cardiovascular systems; persons with other underlying medical conditions, including such metabolic diseases as diabetes, renal dysfunction, and hemoglobinopathies; or persons with known or suspected immunodeficiency diseases or who are receiving immunosuppressive therapies; children or adolescents receiving aspirin or other salicylates (because of the association of Reye syndrome with wild-type influenza infection); persons with a history of Guillain-Barré Syndrome; pregnant women; or persons with a history of hypersensitivity, including anaphylaxis, to any of the components of LAIV or to eggs.

Serious Adverse Events.

Serious adverse events among healthy children aged 5–17 years or healthy adults aged 18–49 years who received LAIV occurred at a rate of $<1\%$. Surveillance should continue for adverse events that might not have been detected in previous studies. Health-care professionals should promptly report all clinically significant adverse events after LAIV (or any vaccine) administration to VAERS. (See **Influenza and Immunization Resources**.)

Influenza Vaccine for Close Contacts of Persons at High Risk for Complications from Influenza

Close contacts of persons at high risk for complications from influenza should receive influenza vaccine to reduce transmission of influenza disease to persons at high risk. Use of inactivated influenza vaccine is preferred for vaccinating household members, HCWs, and others who have close contact with severely immunosuppressed persons (e.g., patients with hematopoietic stem cell transplants) during those periods in which the immunosuppressed person requires care in a protective environment. The rationale for not using LAIV among HCWs caring for such patients is the theoretical risk that a live, attenuated vaccine virus could be transmitted to the severely immunosuppressed person and cause disease. No preference exists for inactivated influenza vaccine use (vs. use of LAIV) by HCWs or other persons who have close contact with persons with lesser degrees of immunosuppression (e.g., persons with diabetes, persons with asthma taking corticosteroids, or persons infected with human immunodeficiency virus), and no preference exists for inactivated influenza vaccine use by HCWs or other healthy persons aged 5–49 years in close contact with all other groups at high risk. If an HCW receives LAIV, that worker should refrain from contact

with severely immunosuppressed patients for 7 days after vaccine receipt. Hospital visitors who have received LAIV should refrain from contact with severely immunosuppressed persons for 7 days after vaccination; however, such persons need not be excluded from visitation of patients who are not severely immunosuppressed.

Optimal Timing of Influenza Vaccine Activities

The optimal time to vaccinate is usually during October–November. ACIP recommends that vaccine providers focus their vaccination efforts in October and earlier primarily on persons aged ≥ 50 years, persons aged <50 years at increased risk for influenza-related complications (including children aged 6–23 months), household contacts of persons at high risk (including out-of-home caregivers and household contacts of children aged 0–23 months) and HCWs. Vaccination of children aged <9 years who are receiving vaccine for the first time should also begin in October or earlier because those persons need a booster dose of the inactivated flu vaccine 1 month after the initial dose, or 6 weeks after if using the LAIV.

To avoid missed opportunities for vaccination of persons at high risk for serious complications, such persons could be offered vaccine beginning in September during routine healthcare visits or during hospitalizations, if vaccine is available. In facilities housing older persons (e.g., nursing homes), vaccination before October typically should be avoided because antibody levels in such persons can begin to decline within a limited time after vaccination. Efforts to vaccinate other persons who wish to decrease their risk for influenza infection should begin in November; however, if such persons request vaccination in October, vaccination should not be deferred.

Timing of Organized Vaccination Campaigns

Persons planning substantial organized vaccination campaigns should consider scheduling these events after mid-October because the availability of vaccine in any location cannot be ensured consistently in early fall. Scheduling campaigns after mid-October will minimize the need for cancellations because vaccine is unavailable. Campaigns conducted before November should focus efforts on vaccination of persons at increased risk for complications and those who are their contacts.

Vaccination in December and Later

After November, many persons who should or want to receive influenza vaccine remain unvaccinated. In addition, substantial amounts of vaccine have remained unused during three of the past four influenza seasons. To improve vaccine coverage, influenza vaccine should continue to be offered in December and throughout the influenza season as long as vaccine supplies are available, even after influenza activity has been documented in the community. In the U.S., seasonal influenza activity may be noted as early as October or November, but influenza activity has not reached peak levels in the majority of recent seasons until late December (as experienced in the 2003–2004 season) through early March. Therefore, although the timing of influenza activity can vary by region, vaccine administered after November is likely to be beneficial in the majority of influenza seasons. Adults

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develop peak antibody protection against influenza infection 2 weeks after vaccination.

Hospitalizations and Deaths from Influenza

The risks for complications, hospitalizations, and deaths from influenza are higher among persons aged ≥65 years, young children, and persons of any age with certain underlying health conditions (see **Persons at Increased Risk for Complications**) than among healthy older children and younger adults. Each year about 114,000 people in the United States are hospitalized and about 36,000 people die because of influenza and its complications. Deaths from influenza are uncommon among children with and without high-risk conditions, but do occur. A study that modeled influenza-related deaths estimated that an average of 92

deaths occurred among children aged <5 years annually during the 1990's compared with 35,274 deaths among adults aged >50 years (1). Preliminary reports of laboratory-confirmed pediatric deaths during the 2003–04 influenza season indicated that among these 143 influenza related deaths (as of April 10, 2004), 58 (41%) were aged <2 years and, of those aged 2–17 years, 65 (45%) did not have an underlying medical condition traditionally considered to place a person at risk for influenza-related complications (unpublished data, CDC National Center for Infectious Diseases, 2004). Further information is needed regarding the risk of severe influenza complications and optimal strategies for minimizing severe disease and death among children.

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Table 2: Recommended Daily Dosage of Influenza Antiviral Medications for Treatment and Prophylaxis

Antiviral agent	Age group (yrs)				
	1–6	7–9	10–12	13–64	≥65
Amantadine* Treatment, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	≤100 mg/day
Rimantadine¶ Treatment,** influenza A	NAT††	NA	NA	100 mg twice daily§ §§	100 mg/day
Prophylaxis, influenza A	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	5 mg/kg body weight/ day up to 150 mg in 2 divided doses†	100 mg twice daily§	100 mg twice daily§	100 mg/day¶¶
Zanamivir*** ††† Treatment, influenza A and B	NA	10 mg twice daily	10 mg twice daily	10 mg twice daily	10 mg twice daily
Oseltamivir Treatment,§§§ influenza A and B	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	Dose varies by child's weight¶¶¶	75 mg twice daily	75 mg twice daily
Prophylaxis, influenza A and B	NA	NA	NA	75 mg/day	75 mg/day

NOTE: Amantadine manufacturers include Endo Pharmaceuticals (Symmetrel® — tablet and syrup); Geneva Pharms Tech and Rosemont (Amantadine HCL — capsule); USL Pharma (Amantadine HCL — capsule and tablet); and Alpharma, Copley Pharmaceutical, HiTech Pharma, Mikart, Morton Grove, Carolina Medical, and Pharmaceutical Associates (Amantadine HCL — syrup). Rimantadine is manufactured by Forest Laboratories (Flumadine® — tablet and syrup) and Corepharma, Impax Labs (Rimantadine HCL — tablet), and Amide Pharmaceuticals (Rimantadine ACL — tablet). Zanamivir is manufactured by GlaxoSmithKline (Relenza® — inhaled powder). Oseltamivir is manufactured by Hoffman-LaRoche, Inc. (Tamiflu® — tablet). This information is based on data published by the Food and Drug Administration (FDA), which is available at <http://www.fda.gov>.

- * The drug package insert should be consulted for dosage recommendations for administering amantadine to persons with creatinine clearance ≤50 mL/min/1.73m².
- † 5 mg/kg body weight of amantadine or rimantadine syrup = 1 tsp/22 lbs.
- § Children aged ≥10 years who weigh <40 kg should be administered amantadine or rimantadine at a dosage of 5 mg/kg body weight/day.
- ¶ A reduction in dosage to 100 mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10 mL/min. Other persons with less severe hepatic or renal dysfunction taking 100 mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.
- ** Only approved by FDA for treatment among adults.
- †† Not applicable.
- §§ Rimantadine is approved by FDA for treatment among adults. However, certain specialists in the management of influenza consider rimantadine appropriate for treatment among children (see American Academy of Pediatrics, 2000 red book: report of the Committee on Infectious Diseases, 25th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2000).
- ¶¶ Older nursing-home residents should be administered only 100 mg/day of rimantadine. A reduction in dosage to 100 mg/day should be considered for all persons aged ≥65 years, if they experience possible side effects when taking 200 mg/day.
- *** Zanamivir is administered through inhalation by using a plastic device included in the medication package. Patients will benefit from instruction and demonstration of correct use of the device.
- ††† Zanamivir is not approved for prophylaxis.
- §§§ A reduction in the dose of oseltamivir is recommended for persons with creatinine clearance <30 mL/min.
- ¶¶¶ The dose recommendation for children who weigh ≤15 kg is 30 mg twice a day. For children who weigh >15–23 kg, the dose is 45 mg twice a day. For children who weigh >23–40 kg, the dose is 60 mg twice a day. And, for children who weigh >40 kg, the dose is 75 mg twice a day.

Cost-Effectiveness of Influenza Vaccine

Influenza vaccination can reduce both health care costs and productivity losses associated with influenza illness. Economic studies of influenza vaccination of persons aged ≥ 65 years conducted in the United States have reported overall societal cost savings and substantial reductions in hospitalization and death. Studies of adults aged < 65 years have reported that vaccination can reduce both direct medical costs and indirect costs from work absenteeism. Reductions of 34%–44% in physician visits, 32%–45% in lost workdays, and 25% in antibiotic use for influenza-associated illnesses have been reported. One cost-effectiveness analysis estimated a cost of approximately \$60–\$4,000/illness averted among healthy persons aged 18–64 years depending on the cost of vaccination, the influenza attack rate, and vaccine effectiveness against influenza-like illness. In a study of inactivated vaccine that included all age groups, cost utility improved with increasing age and among those with chronic medical conditions.

Recommendations for Using Antiviral Agents for Influenza

Antiviral drugs for influenza are an adjunct to influenza vaccine for controlling and preventing influenza. However, these agents are not a substitute for vaccination. Four licensed influenza antiviral agents are available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir. The four drugs differ in pharmacokinetics, side effects, routes of administration, approved age groups, dosages, and costs. An overview of the indications, use, administration, and known primary side effects of these medications is presented in the MMWR. Information contained in that report might not represent FDA approval or approved labeling for the antiviral agents described. Package inserts should be consulted for additional information. Please see Table 2 on the previous page and the MMWR issue for further information.

Role of Laboratory Diagnosis

Appropriate treatment of patients with respiratory illness depends on accurate and timely diagnosis. Early diagnosis of influenza can reduce the inappropriate use of antibiotics and provide the option of using antiviral therapy. However, because certain bacterial infections can produce symptoms similar to influenza, bacterial infections should be considered and appropriately treated, if suspected. In addition, bacterial infections can occur as a complication of influenza. Influenza surveillance information and diagnostic testing can aid clinical judgment and help guide treatment decisions. The accuracy of clinical diagnosis of influenza on the basis of symptoms alone is limited because symptoms from illness caused by other pathogens can overlap considerably with influenza. Influenza surveillance by state and local health departments and CDC can provide information regarding the presence of influenza viruses in the community. Surveillance can also identify the predominant circulating types, subtypes, and strains of influenza. Additional information concerning diagnostic testing is located at <http://www.cdc.gov/flu/professionals/labdiagnosis.htm>. Package inserts and the laboratory performing the test should be consulted for more details regarding use of rapid diagnostic tests.

Physicians and laboratories are encouraged to report positive influenza detections to the County of San Diego Public Health Laboratory by phone (619-692-8500) or fax (619-692-8558) and when possible, to submit specimens for viral culture and isolate subtyping. Surveillance data is available at www.emansandiego.com.

Influenza Vaccine Campaign Offers Opportunity to Provide Other Needed Adult Vaccines

Seniors and others at high risk of complications from influenza visit medical care providers each fall to receive influenza vaccine. Medical care providers should use this opportunity to evaluate these adults for other needed vaccines as well. Vaccines are listed below:

1. Pneumococcal polysaccharide vaccine (PPV-23),
2. Measles, mumps and rubella combination vaccine (MMR),
3. Tetanus and diphtheria vaccine (Td),
4. Varicella vaccine,
5. Hepatitis B vaccine.

Physicians are urged to capitalize on office visits by those at risk for influenza to provide all needed vaccines. To receive a free chart on adult vaccine recommendations, call the Immunization Program at (619) 692-8661.

Influenza and Immunization Resources

The CDC's 2004 report, *Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices (ACIP)*, (Vol. 53, RR-6, May 28, 2004.) includes information on the disease, vaccine, target groups, strategies and the use of antiviral agents in preventing and/or treating influenza. **For a copy of this report, please go to the CDC website noted below or call the Immunization Program at (619) 692-8661.**

The following is a list of World Wide Web sites for accessing information and promotional materials on influenza, influenza vaccine and related topics:

<http://www.cdc.gov/flu> This is the CDC National Immunization Program's flu site, and contains information about vaccine supply, flu treatment and management, a weekly flu activity report, and other items. There is a gallery of patient educational materials developed for the 2004-2005 flu season. The gallery contains downloadable master copies suitable for an office photocopier, and other masters intended for reproduction by commercial printers.

In addition to the CDC's influenza reports mentioned above, this site contains pneumococcal vaccine educational materials and weekly influenza surveillance reports beginning in October. This site has a wide variety of links to other sites with fact sheets for providers and patients.

<http://www.lumetra.com/tools/index.asp>: Lumetra, formerly CMRI, is the designated Quality Improvement Organization (QIO) in California for Medicare. Materials available about flu and pneumonia include information on Medicare billing, and materials on simple proven strategies to reduce flu and pneumonia illnesses. Order online or at 1-800-841-1602.

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www.sdchip.org: This site contains information about Community Health Improvement Partners (CHIP), a collaboration of health care organizations, providers and community groups working in San Diego County to increase awareness of and responsiveness to community health needs. When vaccine becomes available, this web site will feature a list of more than 300 public and private locations in San Diego County where flu shots will be offered. Also, the site has downloadable flu and pneumococcal information in English and 7 other languages, and links to other immunization-related web sites. Flu shot clinic information is also available through CHIP's toll-free number at 1-877-FLU-0202 (1-877-358-0202).

www.immunization-sd.org: The San Diego County Immunization Initiative website contains immunization information specifically for local health care providers, including general immunization recommendations for children and adults, vaccine safety issues, the San Diego Immunization Registry, flu information, as well as the flu shot clinic schedule (when available) at the County Public Health Centers. There are also links to other websites, such as the CDC's influenza information site.

www.immunize.org: The Immunization Action Coalition has a wealth of print materials that can be downloaded and reproduced. Included are childhood and adult materials and official Vaccine Information Statements including, *"Influenza Vaccine, What You Need To Know"* in many languages. VISs are to be given to patients to read before flu vaccine is administered. The California DHS web site has the influenza VIS in English and Spanish with a consent portion attached (www.dhs.ca.gov/ps/dcdc/izgroup/flu.htm).

www.cms.hhs.gov/preventiveservices/2.asp: This is the Centers for Medicare and Medicaid Services (CMS) site about the influenza/pneumococcal campaign. (CMS is the new name of the Health Care Financing Administration.) It also contains information on Medicare, Medicaid and other programs, including how they relate to influenza vaccine.

www.nfid.org: This is the web site of the National Foundation for Infectious Diseases (NFID), which offers information on various infectious diseases and has an "influenza web presentation." Timely and helpful resources with strategies on increasing

influenza immunization rates in infants and children and in HCWs are available on this site. Another part of NFID's site is devoted to the National Coalition for Adult Immunization. It offers adult immunization standards, schedules, recommendations, fact sheets and more. Also, NFID will be promoting the National Adult Immunization Awareness Week from September 26-October 2, 2004.

www2.sdcounty.ca.gov/hhsa/ServiceDetails.asp?ServiceID=826: This is the County of San Diego Health and Human Services Agency website, which has location and contact information for clinics which provide low-cost childhood and adult immunizations. (*Please note that influenza immunization clinic information will probably not be available at this site until early October, when the specifics of the flu shot clinics are finalized.*)

www.vaers.org: This is the website for The Vaccine Adverse Event Reporting System (VAERS). Health care providers and manufacturers are required by law to report suspect reactions to vaccines listed in the Vaccine Injury Table and are encouraged to report even if the vaccines are not listed. VAERS forms are available at 1-800-822-7967 or online at this site.

2004-2005 Influenza Vaccine Manufacturers/Distributors

Aventis-Pasteur, Inc. (Fluzone®) 1-800-VACCINE (1-800-822-2463)

Chiron (Fluvirin®) 1-800-200-4278

MedImmune (FluMist™ LAIV) 1-877-633-4411

Sources

1. Advisory Committee on Immunization Practices, National Immunization Program, Centers for Disease Control and Prevention. *Recommended Childhood and Adolescent Immunization Schedule, United States, July-December 2004.*
2. Advisory Committee on Immunization Practices, National Immunization Program, Centers for Disease Control and Prevention. *Prevention and Control of Influenza, Recommendations of the Advisory Committee on Immunization Practices.* MMWR 2004; Vol. 53:RR-6.
3. Centers for Disease Control and Prevention. *Inactivated Influenza Vaccine, What You Need To Know, 2004-2005.*
4. National Foundation for Infectious Diseases. *Influenza Immunization Among Health Care Workers, Call To Action and Increasing Influenza Immunization Rates in Infants and Children: Putting Recommendations Into Practice.* Both are available at: www.nfid.org.